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MAY 12 2005
PATENT & TRADEMARK OFFICE


```
CTCGAGGACAGTGACCTGGGAGTGAGTACAAGGTGAGGCCACCACTCAGGGT
GCCAGCTCCAAGCGGGTCACAGGGACGAGGGCTGCGGCCATCAGGAGGCCCT
GCACACACATCTGGGACACGCGCCCCCGAGGGCCAGTTCACCTCAGTGCGCC
TCATTCTCCTGCACAAAAGCGCCCCCATCCTTTCTTCACAAGGCTTTCGTGG
AAGCAGAGGCGTCGATGCCCAGTACCCTCTCCCTTTCCCAGGCAACGGGACC
CCAAGTTTGCTGACTGGGACCACCAAGCCACGCATGCGTCAAGAGTGAGAGT
CCGGGACCTAGGCAGGGGCCCTGGGGTTGGGCCTGAGAGAGAAGAGAACCTC
CCCCAGCACTCGGTGTGCATCGGTAGTGAAGGAGCCTCACCTGACCCCCGCT
GTTGCTCAATCGACTTCCCAAGAACAGAGAGAAAAGGGAACTTCCAGGGCGG
CCCGGGCCTCCTGGGGGTTCCCACCCCATTTTTAGCTGAAAGCACTGAGGCA
GAGCTCCCCCTACCCAGGCTCCACTGCCCGGCACAGAAATAACAACCACGGT
TACTGATCATCTGGGAGCTGTCCAGGAATTC
```

FIG._1A

```
  1   GCTGGGCTAA ACTGGGCTAG CCTGAGCTGG GCTGAACTGG GCTGCTGGGC
 51   TGGACTGGGT AAGCTGGGCT GAGCTGGGTT GGGTGGAAAT GGGCTGAGCT
101   GAGCTAGGCT AAACTGGGTT TGGCTGGGCT GGGCTGGGCT GGG
```

FIG._2B

```
  1   GGTTTGGCTG GGCTGGGCTG GGCTGGGCTG GGTTCAGCTG AGCGGGTTGG
 51   GTTAGACTGG GTCAAACTGG TTCAGC
```

FIG._2C

BEST AVAILABLE COPY

GERMLINE & LOCUS

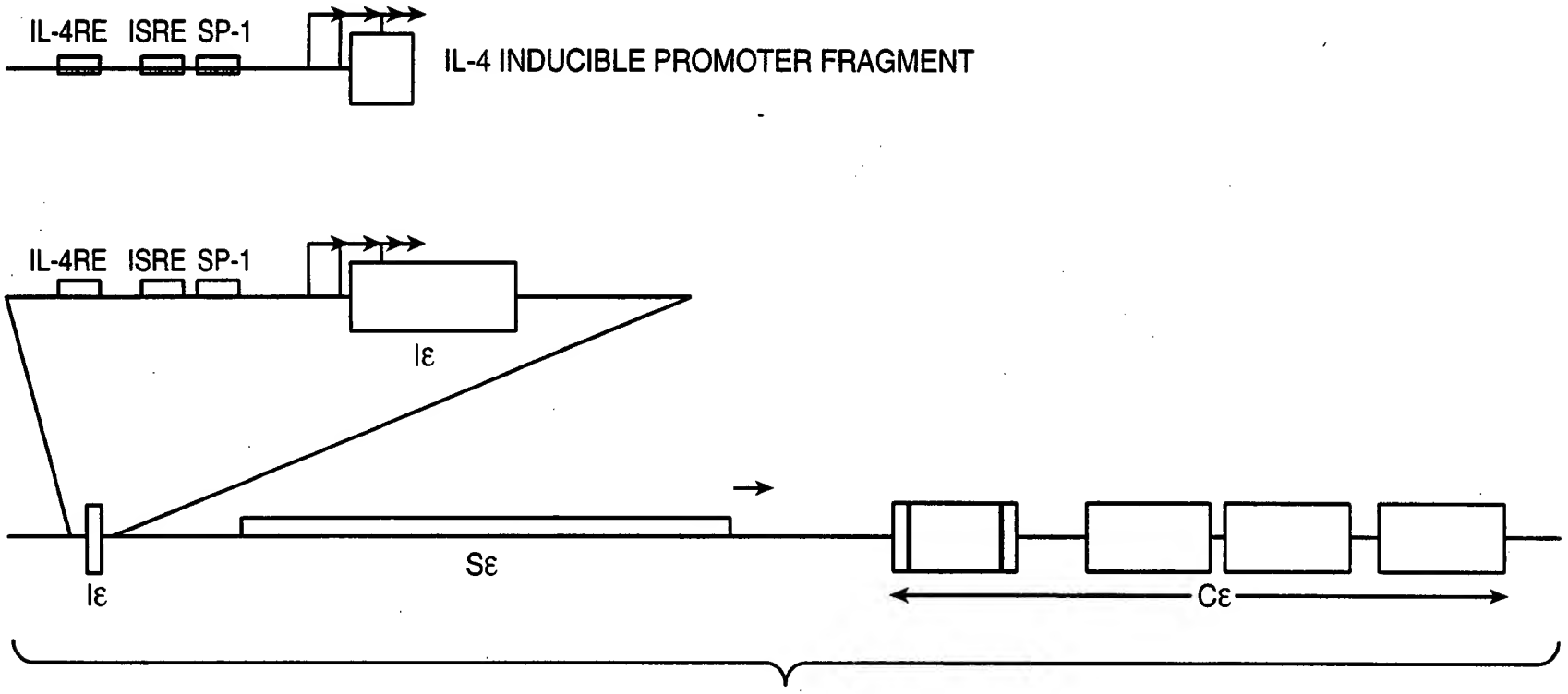
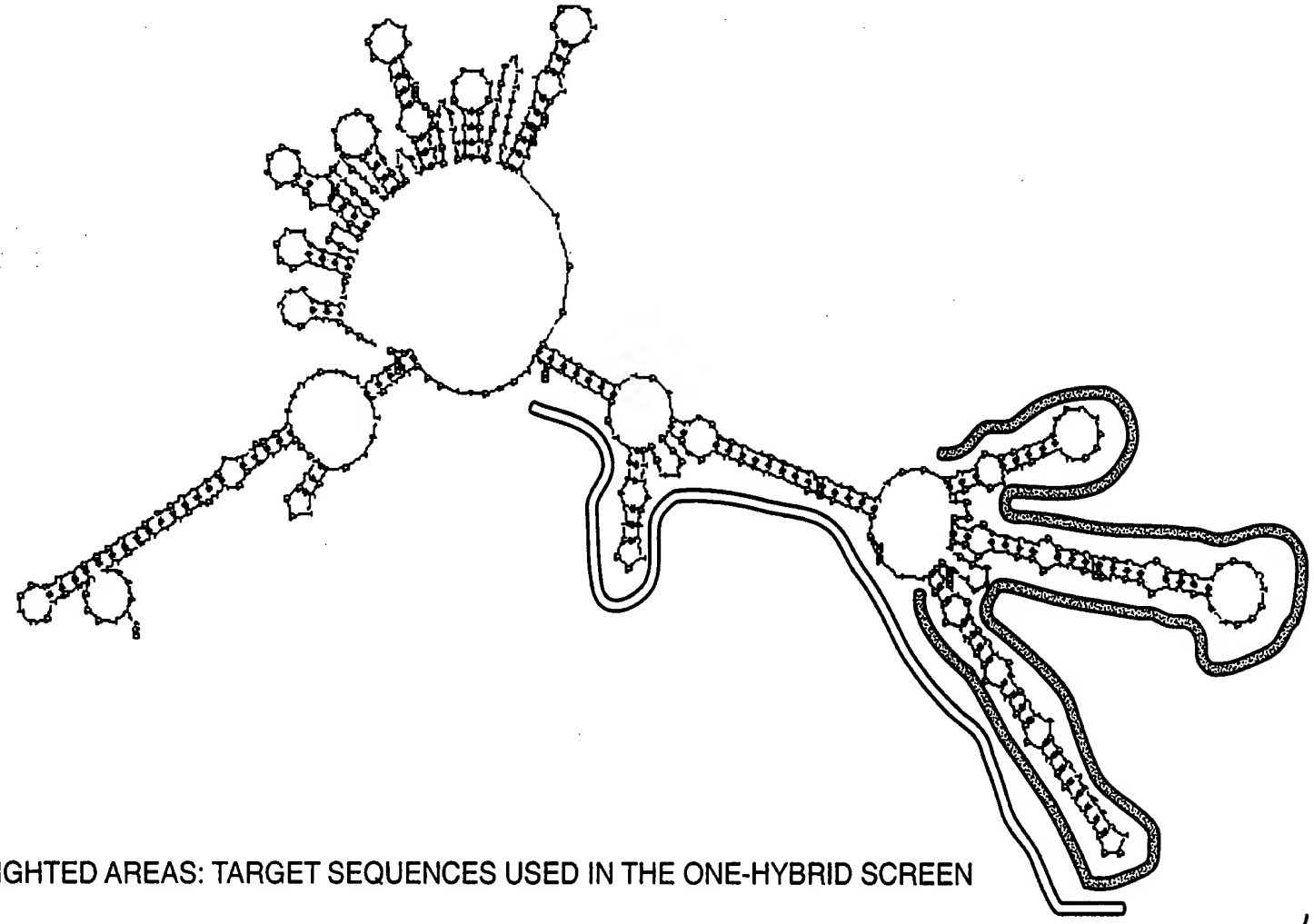


FIG._1B

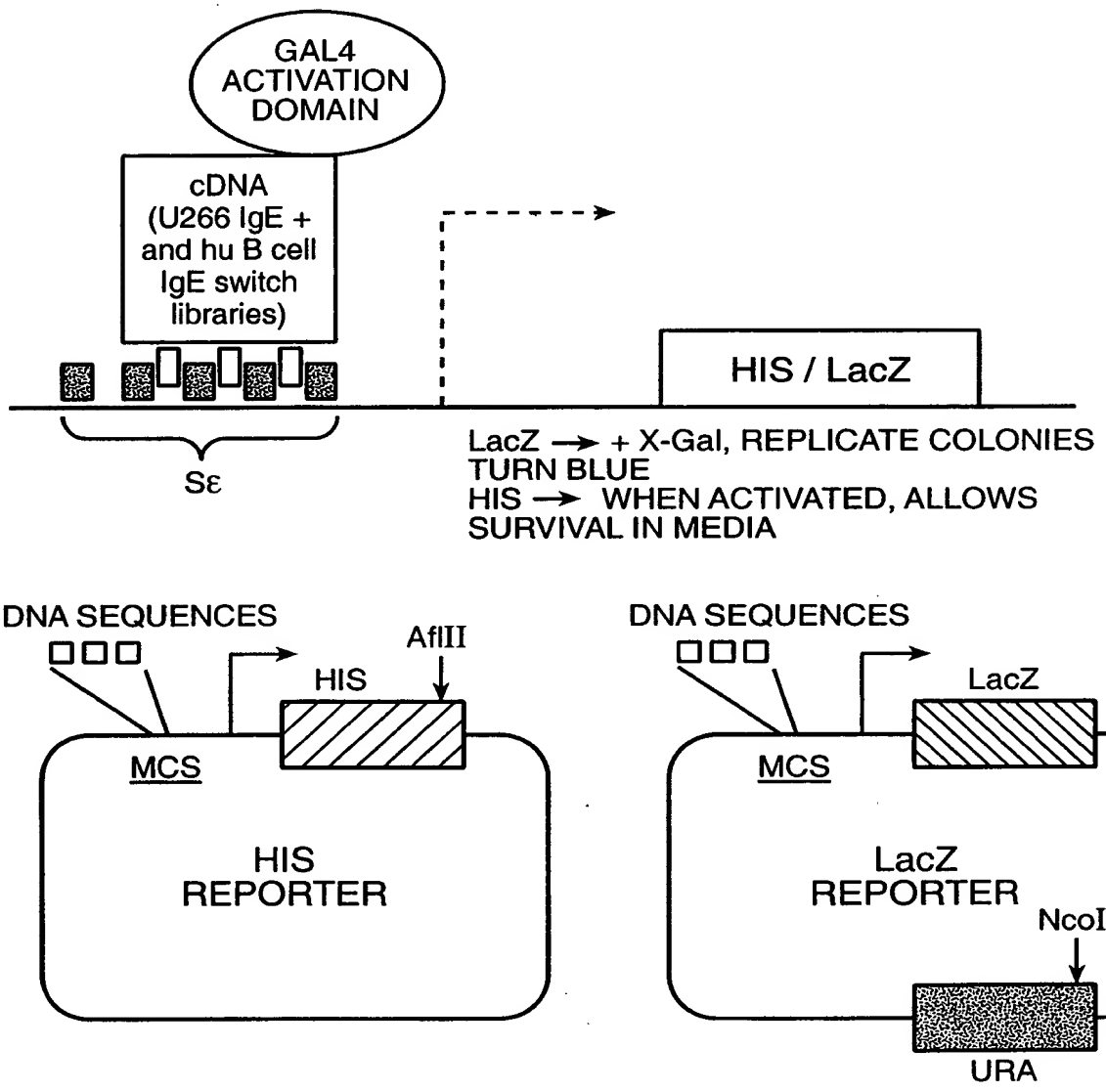
LOW ENERGY DNA FOLDING OF THE Sε REGION



HIGHLIGHTED AREAS: TARGET SEQUENCES USED IN THE ONE-HYBRID SCREEN

FIG._2A

YEAST ONE-HYBRID SCREENING



ONE HYBRID REPORTER VECTORS
DNA SEQUENCES OF INTEREST ARE INSERTED INTO THE MULTIPLE CLONING SITES (MCS). THE ENZYME USED TO LINEARIZE THE VECTOR IS SHOWN WITH A SOLID ARROW. DASHED ARROWS INDICATE THE TRANSCRIPTION OF THE REPORTER GENE.

FIG._3

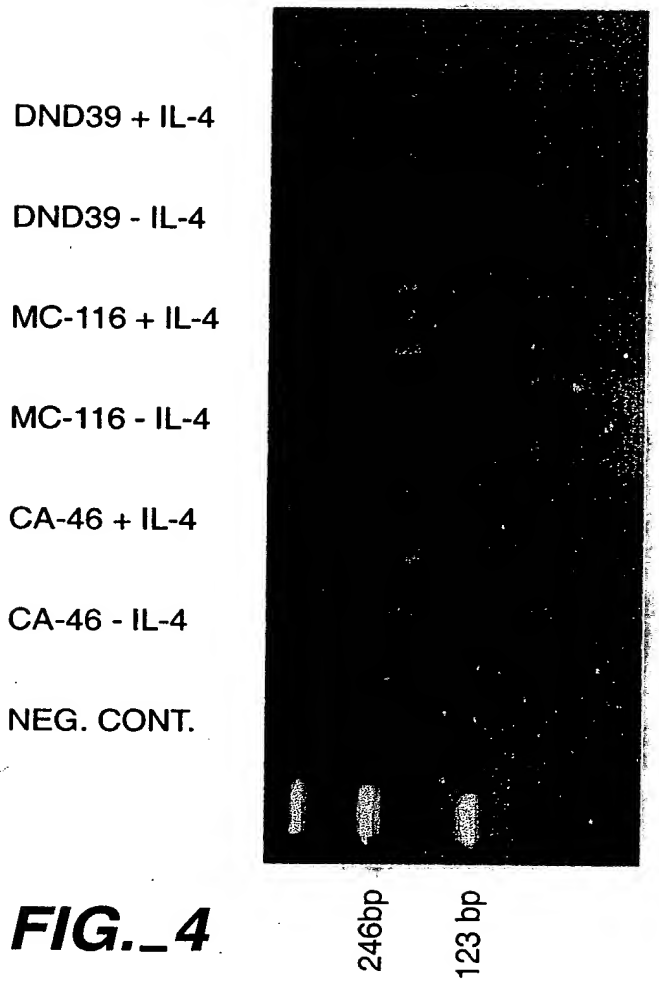

DND39 + IL-4
DND39 - IL-4
MC-116 + IL-4
MC-116 - IL-4
CA-46 + IL-4
CA-46 - IL-4
NEG. CONT.
246bp
123 bp

FIG._4

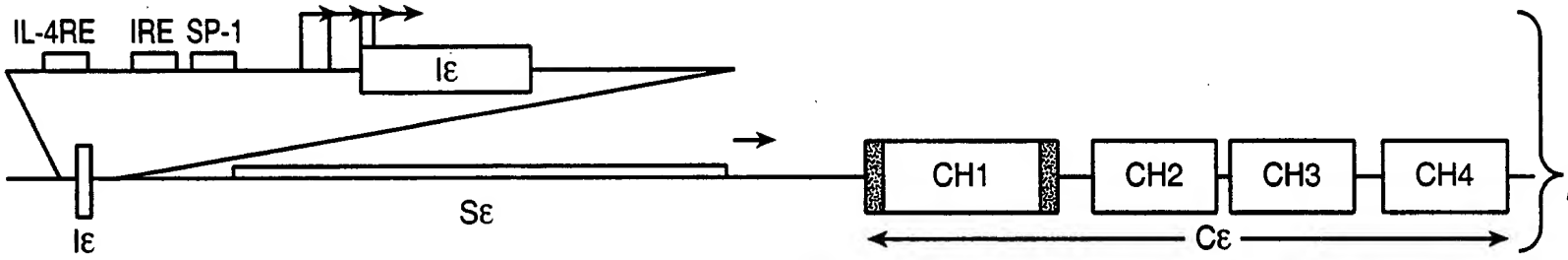


FIG._5A

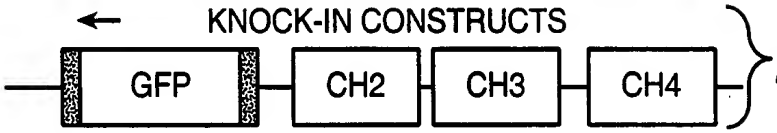


FIG._5B

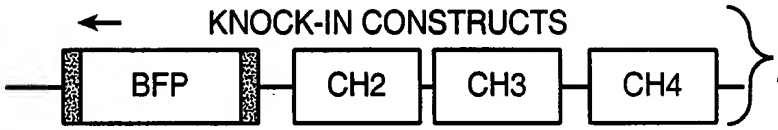


FIG._5C

IL-4 RE, IL-4 RESPONSIVE ELEMENT
IRE, INTERFERON RESPONSIVE ELEMENT
SP-1, SP-1 BINDING SITE
Iε, NON-TRANSLATED EXON
Sε, SWITCH REGION OF ε
GFP, GREEN FLUORESCENT PROTEIN
BFP, BLUE FLUORESCENT PROTEIN
CH1,2,3,4, CONSTANT REGION DOMAIN EXONS

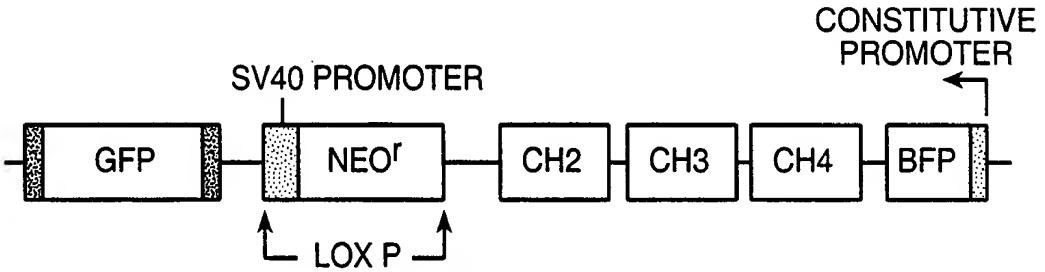


FIG._5D

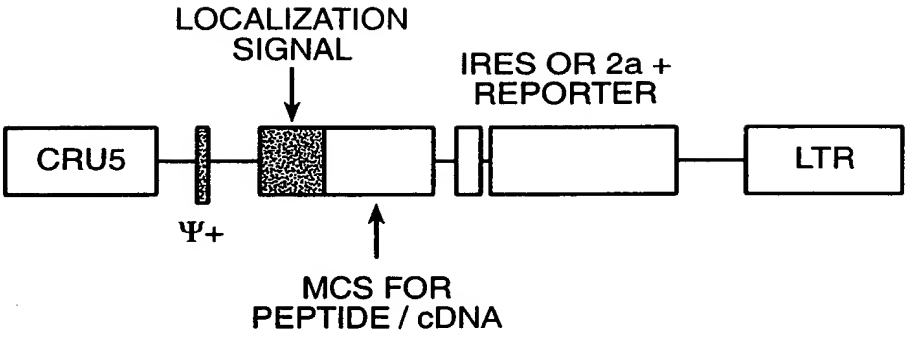

LOCALIZATION
SIGNAL
IRES OR 2a +
REPORTER
CRU5
LTR
Ψ+
MCS FOR
PEPTIDE / cDNA

FIG._6

PROTOCOL FOR TRANSFECTION OF PHOENIX CELLS
AND INFECTION OF NONADHERENT TARGET CELLS

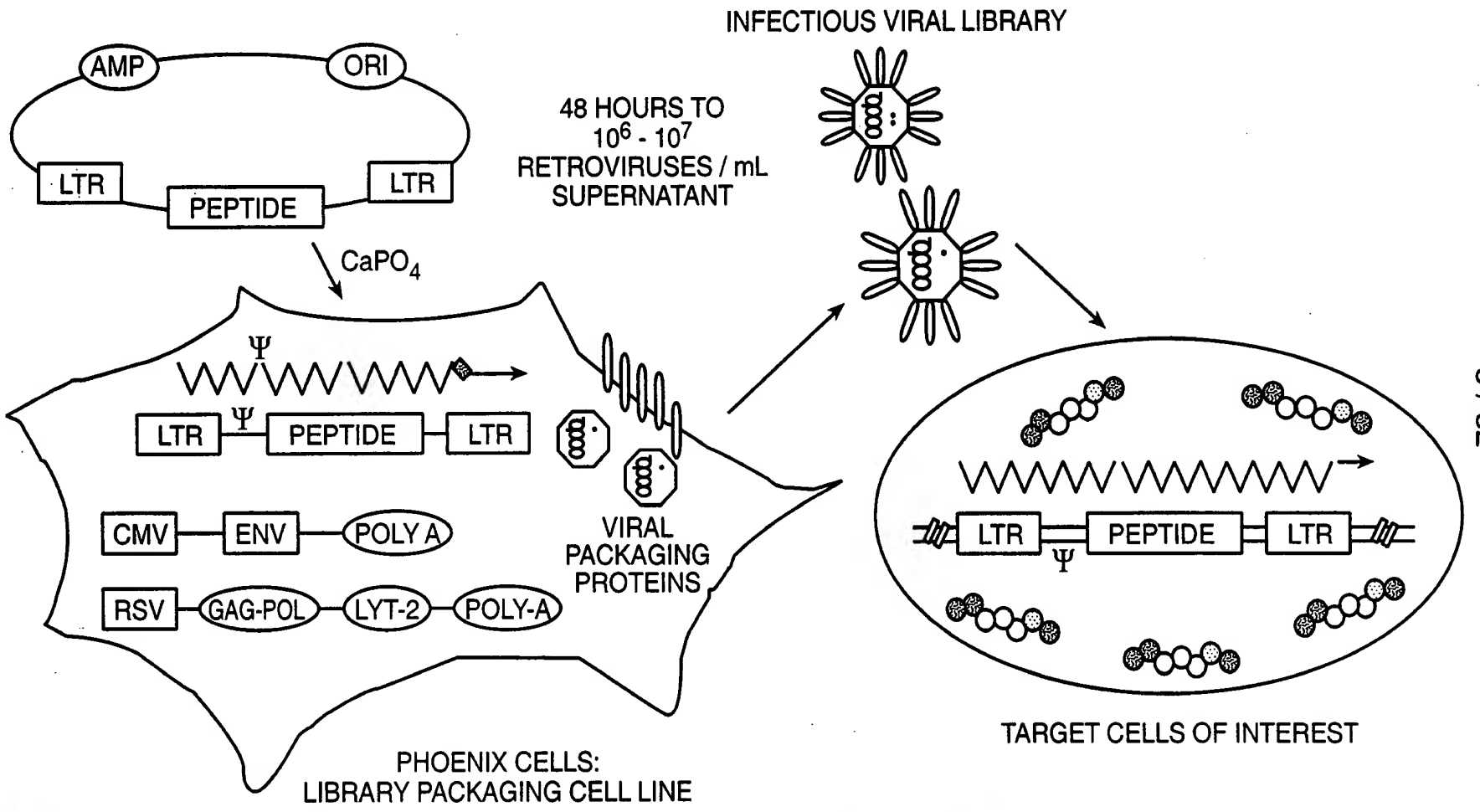


FIG._7

ε HEAVY CHAIN GFP / BFP KNOCK-IN CELL LINE

U266 ε HEAVY CHAIN

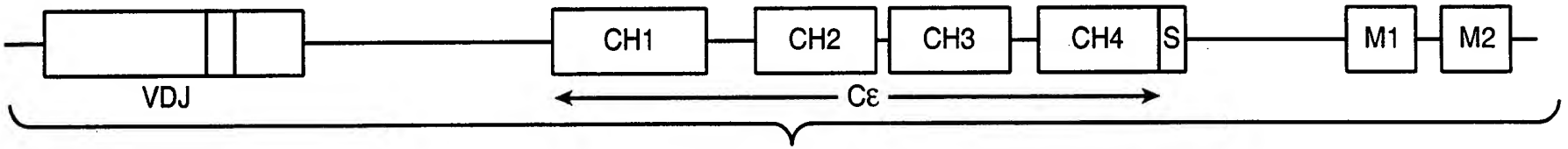
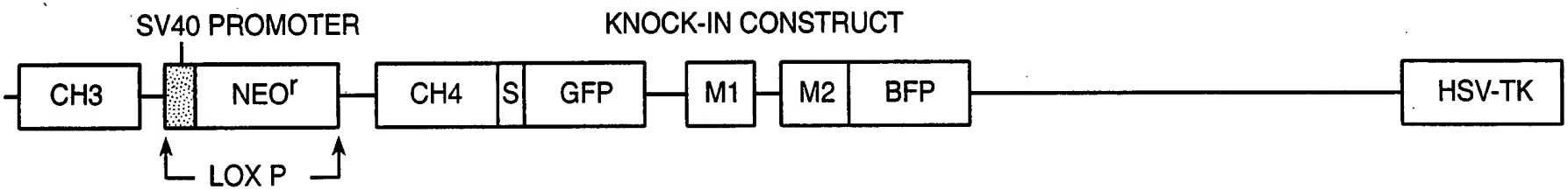


FIG._8A



U266 CELLS ARE TRANSFECTED AND SELECTED WITH G418. SURVIVORS ARE TREATED WITH GANCICLOVIR (HSV-TK DELETED DURING HOMOLOGOUS RECOMBINATION). RT-PCR IS PERFORMED TO CONFIRM HOMOLOGOUS RECOMBINATION. THOSE CLONES ARE TRANSFECTED WITH *cre* TO REMOVE THE SV40 NEOMYCIN RESISTANCE GENE.

FIG._8B

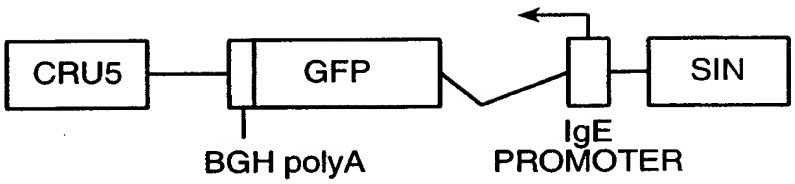

CRU5
GFP
SIN
BGH polyA
IgE
PROMOTER

FIG._9A

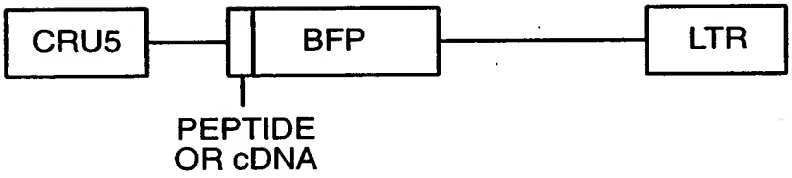

CRU5
BFP
LTR
PEPTIDE
OR cDNA

FIG._9B

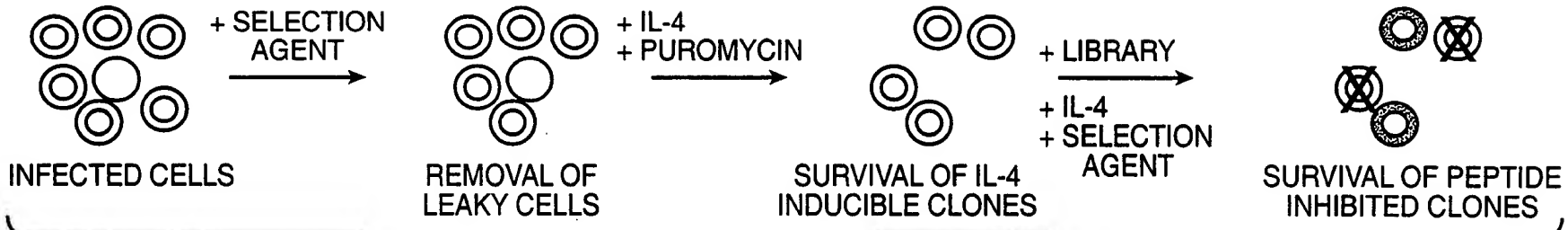
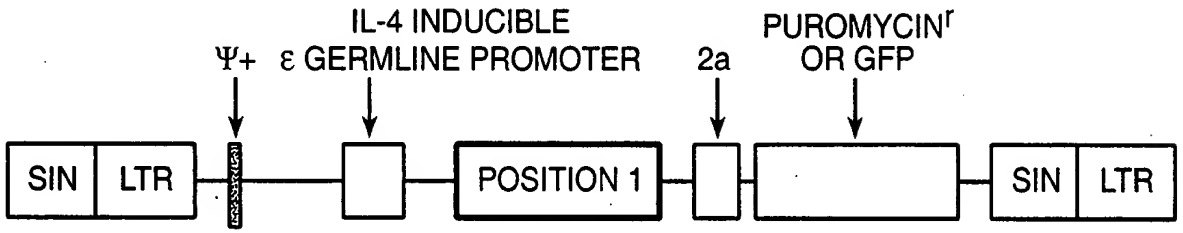


FIG._10A



+ DEATH INDUCER

SELECTION AGENT
αFAS

GANCICLOVIR
CYCLOPHOSPHAMIDE
NONE (SELF SELECTION)

ALL COMPONENTS ARE CASSETTED FOR FLEXIBILITY

FIG._10B

1-845 CMV promoter/R/U5 5' LTR
1322 GAG ATG-ATC mutation
850-2100 extended Ψ region
2146-2173 two Bstx1 peptide cloning sites
2205-2723 ECMV IRES (cloned as EcoR1/Msc1 fragment from pCITE-4a [Novagen])
2746-3465 GFP coding region
3522-4115 3' LTR
4122-6210 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATCC
CAAACTCAAATATATAAAGCATTTGACTTGTTCTATGCCCTAGTTATTAATAGTAATCAA
TTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTAA
ATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTATG
TTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACGGT
AAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACG
TCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTC
CTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGC
AGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCA
TTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTA
ACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCATGTACGGTGGGAGGTCTATATAA
GCAGAGCTCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCCAGTCCTCCGATTGACT
GAGTCGCCCGGGTACCCGTGTATCCAATAAACCCTCTTGCAGTTGCATCCGACTTGTGGT
CTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTT
CATTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCCAGGGACCACCGACCCACCACCG
GGAGGTAAGCTGGCCAGCAACTTATCTGTGTCTGTCCGATTGTCTAGTGTCTATGACTGA
TTTTATGCGCCTGCGTCGGTACTAGTTAGCTAACTAGCTCTGTATCTGGCGGACCCGTGG
TGGAACTGACGAGTTCGGAACACCCGGCCGCAACCCTGGGAGACGTCCCAGGGACTTCGG
GGGCCGTTTTTGTGGCCCGACCTGAGTCCAAAAATCCCGATCGTTTTGGACTCTTTGGTG
CACCCCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGACGAGAACCTAAAACAGTTCC
CGCCTCCGTCTGAATTTTTGCTTTCGGTTTGGGACCGAAGCCGCGCCGCGCGTCTTGTCT
GCTGCAGCATCGTTCTGTGTTGTCTCTGTCTGACTGTGTTTCTGTATTTGTCTGAAAATA
TCGGCCCGGGCCAGACTGTTACCACTCCCTTAAGTTTGACCTTAGGTCACTGGAAAGATG
TCGAGCGGATCGCTCACAACCAGTCGGTAGATGTCAAGAAGAGACGTTGGGTTACCTTCT
GCTCTGCAGAATGGCCAACCTTTAACGTCGGATGGCCGCGAGACGGCACCTTTAACCGAG
ACCTCATCACCCAGGTTAAGATCAAGGTCTTTTCACCTGGCCCGCATGGACACCCAGACC
AGGTCCCCTACATCGTGACCTGGGAAGCCTTGGCTTTTGACCCCCCTCCCTGGGTCAAGC
CCTTTGTACACCCTAAGCCTCCGCCTCCTCTTCCTCCATCCGCCCCGTCTCTCCCCCTTG
AACCTCCTCGTTCGACCCCGCCTCGATCCTCCCTTTATCCAGCCCTCACTCCTTCTCTAG
GCGCCCCCATATGGCCATATGAGATCTTATATGGGGCACCCCCGCCCCTTGTAAACTTCC
CTGACCCTGACATGACAAGAGTTACTAACAGCCCCTCTCTCCAAGCTCACTTACAGGCTC
TCTACTTAGTCCAGCACGAAGTCTGGAGACCTCTGGCGGCAGCCTACCAAGAACAACTGG
ACCGACCGGTGGTACCTCACCCTTACCGAGTCGGCGACACAGTGTGGGTCCGCCGACACC
AGACTAAGAACCTAGAACCTCGCTGGAAAGGACCTTACACAGTCCTGCTGACCACCCCCA
CCGCCCTCAAAGTAGACGGCATCGCGCTTGGATACACGCCGCCCACGTGAAGGCTGCCGA
CCCCGGGGGTGGACCATCCTCTAGACTGCCGGATCTCGAGGGATCCACCACCATGGACCC
CCATTAAATTGGAATTCCTGCAGCCCGGGGGATCCACTAGTTCTAGAGCGAATTAATTCC

FIG._11A-1

GGTTATTTTCCACCATATTGCCGTCTTTTGGCAATGTGAGGGCCCGGAAACCTGGCCCTG
TCTTCTTGACGAGCATTCCTAGGGGTCTTTCCCCTCTCGCCAAAGGAATGCAAGGTCTGT
TGAATGTCGTGAAGGAAGCAGTTCCTCTGGAAGCTTCTTGAAGACAAACAACGTCTGTAG
CGACCCTTTGCAGGCAGCGGAACCCCCCACCTGGCGACAGGTGCCTCTGCGGCCAAAAGC
CACGTGTATAAGATACACCTGCAAAGGCGGCACAACCCCAGTGCCACGTTGTGAGTTGGA
TAGTTGTGGAAAGAGTCAAATGGCTCTCCTCAAGCGTATTCAACAAGGGGCTGAAGGATG
CCCAGAAGGTACCCCATTGTATGGGATCTGATCTGGGGCCTCGGTGCACATGCTTTACAT
GTGTTTAGTCGAGGTTAAAAAACGTCTAGGCCCCCCGAACCACGGGGACGTGGTTTTCCT
TTGAAAAACACGATGATAATATGGGGGATCCACCGGTCGCCACCATGGTGAGCAAGGGCG
AGGAGCTGTTCACCGGGGTGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAACGGCC
ACAAGTTCAGCGTGTCCGGCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCTGA
AGTTCATCTGCACCACCGGCAAGCTGCCCGTGCCCTGGCCCACCCTCGTGACCACCCTGA
CCTACGGCGTGCAGTGCTTCAGCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCA
AGTCCGCCATGCCCGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACGACGGCA
ACTACAAGACCCGCGCCGAGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGC
TGAAGGGCATCGACTTCAAGGAGGACGGCAACATCCTGGGGCACAAGCTGGAGTACAACT
ACAACAGCCACAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATCAAGGTGAACT
TCAAGATCCGCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCAGCAGA
ACACCCCCATCGGCGACGGCCCCGTGCTGCTGCCCGACAACCACTACCTGAGCACCCAGT
CCGCCCTGAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTCCTGCTGGAGTTCGTGA
CCGCCGCCGGGATCACTCTCGGCATGGACGAGCTGTACAAGTAAAGCGGCCGCTCGACGA
TAAAATAAAAGATTTTATTTAGTCTCCAGAAAAAGGGGGGAATGAAAGACCCCACCTGTA
GGTTTGGCAAGCTAGCTTAAGTAACGCCATTTTGCAAGGCATGGAAAAATACATAACTGA
GAATAGAGAAGTTCAGATCAAGGTCAGGAACAGATGGAACAGCTGAATATGGGCCAAACA
GGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGAACAGCTG
AATATGGGCCAAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAA
CAGATGGTCCCCAGATGCGGTCCAGCCCTCAGCAGTTTCTAGAGAACCATCAGATGTTTC
CAGGGTGCCCCAAGGACCTGAAATGACCCTGTGCCTTATTTGAACTAACCAATCAGTTCG
CTTCTCGCTTCTGTTCGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGCCCACAACCCC
TCACTCGGGGCGCCAGTCCTCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAA
ACCCTCTTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGA
GTGATTGACTACCCGTCAGCGGGGGTCTTTCATTTCCGACTTGTGGTCTCGCTGCCTTGG
GAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTCACATGCAGCATGTAT
CAAAATTAATTTGGTTTTTTTTCTTAAGTATTTACATTAAATGGCCATAGTTGCATTAAT
GAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGCGCTCTTCCGCTTCCTCGCT
CACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGC
GGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGG
CCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCG
CCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGG
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CCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCA
TAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGT
GCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTC
CAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAG
AGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACAC

FIG._11A-2

TAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGT
TGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAA
GCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGG
GTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAA
AAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTGCGCAAATCAATCTAAAG
TATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTC
AGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTAC
GATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTC
ACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGG
TCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAG
TAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTC
ACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTAC
ATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAG
AAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTAC
TGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTG
AGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAACACGGGATAATACCGC
GCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACT
CTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTG
ATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAA
TGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTT
TCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATG
TATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTC

FIG._11A-3

1-845 CMVpormoter/R/U5 5' LTR
1322 GAG ATG-ATC mutation
850-2100 extended □ region
2151-2865 GFP coding region
2866-2894 GGGSGGG linker
2895-2952 FMDV 2a cleavage sequence
2953-3004 Bstx1/Bstx1/HinD3/Hpa1/Sal1/Not1 polylinker
3052-3645 3' LTR
3652-5715 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATC
CCAAACTCAAATATATAAAGCATTTGACTTGTTCTATGCCCTAGTTATTAATAGTAATC
AATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGG
TAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACG
TATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTT
ACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTA
TTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGG
GACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCG
GTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTC
TCCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCA
AAATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCATGTACGGTGGGA
GGTCTATATAAGCAGAGCTCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCCAGTC
CTCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAAACCCTCTTGCAGTTGCA
TCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGT
CAGCGGGGGTCTTTCATTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCCAGGGACC
ACCGACCCACCACCGGGAGGTAAGCTGGCCAGCAACTTATCTGTGTCTGTCCGATTGTC
TAGTGTCTATGACTGATTTTATGCGCCTGCGTCGGTACTAGTTAGCTAACTAGCTCTGT
ATCTGGCGGACCCGTGGTGGAACTGACGAGTTCGGAACACCCGGCCGCAACCCTGGGAG
ACGTCCCAGGGACTTCGGGGGCCGTTTTTGTGGCCCGACCTGAGTCCAAAAATCCCGAT
CGTTTTGGACTCTTTGGTGCACCCCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGA
CGAGAACCTAAAACAGTTCCCGCCTCCGTCTGAATTTTTGCTTTCGGTTTGGGACCGAA
GCCGCGCCGCGCGTCTTGTCTGCTGCAGCATCGTTCTGTGTTGTCTCTGTCTGACTGTG
TTTCTGTATTTGTCTGAAAATATCGGCCCGGGCCAGACTGTTACCACTCCCTTAAGTTT
GACCTTAGGTCACTGGAAAGATGTCGAGCGGATCGCTCACAACCAGTCGGTAGATGTCA
AGAAGAGACGTTGGGTTACCTTCTGCTCTGCAGAATGGCCAACCTTTAACGTCGGATGG
CCGCGAGACGGCACCTTTAACCGAGACCTCATCACCCAGGTTAAGATCAAGGTCTTTTC
ACCTGGCCCGCATGGACACCCAGACCAGGTCCCCTACATCGTGACCTGGGAAGCCTTGG
CTTTTGACCCCCCTCCCTGGGTCAAGCCCTTTGTACACCCTAAGCCTCCGCCTCCTCTT
CCTCCATCCGCCCCGTCTCTCCCCCTTGAACCTCCTCGTTCGACCCCGCCTCGATCCTC
CCTTTATCCAGCCCTCACTCCTTCTCTAGGCGCCCCCATATGGCCATATGAGATCTTAT
ATGGGGCACCCCCGCCCCTTGTAAACTTCCCTGACCCTGACATGACAAGAGTTACTAAC
AGCCCCTCTCTCCAAGCTCACTTACAGGCTCTCTACTTAGTCCAGCACGAAGTCTGGAG
ACCTCTGGCGGCAGCCTACCAAGAACAACTGGACCGACCGGTGGTACCTCACCCTTACC
GAGTCGGCGACACAGTGTGGGTCCGCCGACACCAGACTAAGAACCTAGAACCTCGCTGG
AAAGGACCTTACACAGTCCTGCTGACCACCCCCACCGCCCTCAAAGTAGACGGCATCGC
AGCTTGGATACACGCCGCCCACGTGAAGGCTGCCGACCCCGGGGGGTGGACCATCCTCTA
GACTGCCGGATCTCGAGGGATCCACCATGGTGAGCAAGGGCGAGGAGCTGTTCACCGGG

FIG._11B-1

GTGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAACGGCCACAAGTTCAGCGTGTC
CGGCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCTGAAGTTCATCTGCACCA
CCGGCAAGCTGCCCGTGCCCTGGCCCACCCTCGTGACCACCCTGACCTACGGCGTGCAG
TGCTTCAGCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCAAGTCCGCCATGCC
CGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACGACGGCAACTACAAGACCC
GCGCCGAGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGCTGAAGGGCATC
GACTTCAAGGAGGACGGCAACATCCTGGGGCACAAGCTGGAGTACAACTACAACAGCCA
CAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATCAAGGTGAACTTCAAGATCC
GCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCAGCAGAACACCCCC
ATCGGCGACGGCCCCGTGCTGCTGCCCGACAACCACTACCTGAGCACCCAGTCCGCCCT
GAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTCCTGCTGGAGTTCGTGACCGCCG
CCGGGATCACTCTCGGCATGGACGAGCTGTACAAGGAATTCGGAGGTGGCAGCGGTGGC
GGTCAGCTGTTGAATTTTGACCTTCTTAAACTTGCGGGAGACGTCGAGTCCAACCCTGG
GCCCACCACCACCATGGAAGCTTCCATTAAATTGGTTAACGTCGACGCGGCCGCTCGAC
GATAAAATAAAAGATTTTATTTAGTCTCCAGAAAAAGGGGGGAATGAAAGACCCCACCT
GTAGGTTTGGCAAGCTAGCTTAAGTAACGCCATTTTGCAAGGCATGGAAAAATACATAA
CTGAGAATAGAGAAGTTCAGATCAAGGTCAGGAACAGATGGAACAGCTGAATATGGGCC
AAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGAA
CAGCTGAATATGGGCCAAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGG
CCAAGAACAGATGGTCCCCAGATGCGGTCCAGCCCTCAGCAGTTTCTAGAGAACCATCA
GATGTTTCCAGGGTGCCCCAAGGACCTGAAATGACCCTGTGCCTTATTTGAACTAACCA
ATCAGTTCGCTTCTCGCTTCTGTTCGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGC
CCACAACCCCTCACTCGGGGCGCCAGTCCTCCGATTGACTGAGTCGCCCGGGTACCCGT
GTATCCAATAAACCCTCTTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAG
GGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTTCATTTCCGACTTGTGGT
CTCGCTGCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTCA
CATGCAGCATGTATCAAAATTAATTTGGTTTTTTTTCTTAAGTATTTACATTAAATGGC
CATAGTTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGCGCT
CTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTA
TCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAA
GAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGG
CGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAG
AGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCT
CGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTT
CGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTC
GTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTT
ATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAG
CAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTG
AAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCT
GAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCG
CTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCT
CAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACG
TTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATT
AAAAATGAAGTTTGCGCAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGT
TACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCAT
AGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCC
CCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATA

FIG._11B-2

AACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCAT
CCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGC
GCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTTGGTATGGCT
TCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAA
AAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGT
TATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGA
TGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCG
ACCGAGTTGCTCTTGCCCGGCGTCAACACGGGATAATACCGCGCCACATAGCAGAACTT
TAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCG
CTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTT
TACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGG
GAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGA
AGCATTTATCAGGGTTATTGTCTCATGACATTAACCTATAAAAATAGGCGT

FIG._11B-3

1-845 CMVpormoter/R/U5 5' LTR
1322 GAG ATG-ATC mutation
850-2100 extended $\bar{-}$ region
2146-2173 two Bstx1 peptide cloning sites
2173-2214 EoR1/Apa1/Hpa1/Not1 polylinker
2262-2855 3' LTR
2855-4901 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATC
CCAAACTCAAATATATAAAGCATTTGACTTGTTCTATGCCCTAGTTATTAATAGTAATC
AATTACGGGGTCATTAGTTCATAGCCATATATGGAGTTCCGCGTTACATAACTTACGGT
AAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGT
ATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTA
CGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTAT
TGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGG
ACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGG
TTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCT
CCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAA
AATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCATGTACGGTGGGAG
GTCTATATAAGCAGAGCTCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCCAGTCC
TCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAAACCCTCTTGCAGTTGCAT
CCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTC
AGCGGGGGTCTTTCATTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCCAGGGACCA
CCGACCCACCACCGGGAGGTAAGCTGGCCAGCAACTTATCTGTGTCTGTCCGATTGTCT
AGTGTCTATGACTGATTTTATGCGCCTGCGTCGGTACTAGTTAGCTAACTAGCTCTGTA
TCTGGCGGACCCGTGGTGGAACTGACGAGTTCGGAACACCCGGCCGCAACCCTGGGAGA
CGTCCCAGGGACTTCGGGGGCCGTTTTTGTGGCCCGACCTGAGTCCAAAAATCCCGATC
GTTTTGGACTCTTTGGTGCACCCCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGAC
GAGAACCTAAAACAGTTCCCGCCTCCGTCTGAATTTTTGCTTTCGGTTTGGGACCGAAG
CCGCGCCGCGCGTCTTGTCTGCTGCAGCATCGTTCTGTGTTGTCTCTGTCTGACTGTGT
TTCTGTATTTGTCTGAAAATATCGGCCCGGGCCAGACTGTTACCACTCCCTTAAGTTTG
ACCTTAGGTCACTGGAAAGATGTCGAGCGGATCGCTCACAACCAGTCGGTAGATGTCAA
GAAGAGACGTTGGGTTACCTTCTGCTCTGCAGAATGGCCAACCTTTAACGTCGGATGGC
CGCGAGACGGCACCTTTAACCGAGACCTCATCACCCAGGTTAAGATCAAGGTCTTTTCA
CCTGGCCCGCATGGACACCCAGACCAGGTCCCCTACATCGTGACCTGGGAAGCCTTGGC
TTTTGACCCCCCTCCCTGGGTCAAGCCCTTTGTACACCCTAAGCCTCCGCCTCCTCTTC
CTCCATCCGCCCCGTCTCTCCCCCTTGAACCTCCTCGTTCGACCCCGCCTCGATCCTCC
CTTTATCCAGCCCTCACTCCTTCTCTAGGCGCCCCCATATGGCCATATGAGATCTTATA
TGGGGCACCCCCGCCCCTTGTAAACTTCCCTGACCCTGACATGACAAGAGTTACTAACA
GCCCCTCTCTCCAAGCTCACTTACAGGCTCTCTACTTAGTCCAGCACGAAGTCTGGAGA
CCTCTGGCGGCAGCCTACCAAGAACAACTGGACCGACCGGTGGTACCTCACCCTTACCG
AGTCGGCGACACAGTGTGGGTCCGCCGACACCAGACTAAGAACCTAGAACCTCGCTGGA
AAGGACCTTACACAGTCCTGCTGACCACCCCCACCGCCCTCAAAGTAGACGGCATCGCA
GCTTGGATACACGCCGCCCACGTGAAGGCTGCCGACCCCGGGGGTGGACCATCCTCTAG
ACTGCCGGATCTCGAGGGATCCACCACCATGGACCCCCATTAAATTGGAATTCGGGGCC
CAAGCTTTGTTAACGTCGACGCGGCCGCCGTCGACGATAAAATAAAAGATTTTATTTAG
TCTCCAGAAAAAGGGGGGAATGAAAGACCCCACCTGTAGGTTTGGCAAGCTAGCTTAAG
TAACGCCATTTTGCAAGGCATGGAAAAATACATAACTGAGAATAGAGAAGTTCAGATCA

FIG._11C-1

AGGTCAGGAACAGATGGAACAGCTGAATATGGGCCAAACAGGATATCTGTGGTAAGCAG
TTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGAACAGCTGAATATGGGCCAAACAGGA
TATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGTCCCCAGATG
CGGTCCAGCCCTCAGCAGTTTCTAGAGAACCATCAGATGTTTCCAGGGTGCCCCAAGGA
CCTGAAATGACCCTGTGCCTTATTTGAACTAACCAATCAGTTCGCTTCTCGCTTCTGTT
CGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCC
AGTCCTCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAAACCCTCTTGCAGT
TGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTAC
CCGTCAGCGGGGGTCTTTCATTTCCGACTTGTGGTCTCGCTGCCTTGGGAGGGTCTCCT
CTGAGTGATTGACTACCCGTCAGCGGGGGTCTTCACATGCAGCATGTATCAAAATTAAT
TTGGTTTTTTTTCTTAAGTATTTACATTAAATGGCCATAGTTGCATTAATGAATCGGCC
AACGCGCGGGGAGAGGCGGTTTGCGTATTGGCGCTCTTCCGCTTCCTCGCTCACTGACT
CGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATA
CGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCA
AAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCC
CTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTA
TAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCT
GCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATA
GCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTG
CACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTC
CAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCA
GAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTAC
ACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAG
AGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTT
GCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCT
ACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATT
ATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTGCGCAAATCAA
TCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCA
CCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTA
GATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAG
ACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAG
CGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGA
AGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAG
GCATCGTGGTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGA
TCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCC
TCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCAC
TGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTAC
TCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTC
AACACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAAC
GTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAA
CCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTG
AGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTT
GAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTC
ATGACATTAACCTATAAAAATAGGCGT

FIG._11C-2

atcacgaggccctttcgtcttcaagaacagctttgctcttaggagtttcctaatacatcccaaactcaaatatataaagc
atttgacttgttctatgccctagttattaatagtaatcaattacggggtcattagttcatagcccatatatggagttccg
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ttcccatagtaacgccaatagggactttccattgacgtcaatgggtggagtatttacggtaaactgcccacttggcagta
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ttttggcaccaaaatcaacgggactttccaaaatgtcgtaacaactccgccccattgacgcaaatgggcggtaggcatgt
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gagtcgcccgggtacccgtgtatccaataaaccctcttgcagttgcatccgacttgtggtctcgctgttccttgggaggg
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ggaccaccgacccaccaccgggaggtaagctggccagcaacttatctgtgtctgtccgattgtctagtgtctatgactga
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cacccggccgcaaccctgggagacgtcccagggacttcgggggccgtttttgtggcccgacctgagtccaaaaatcccga
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gctctgcagaatggccaacctttaacgtcggatggccgcgagacggcacctttaaccgagacctcatcacccaggttaag
atcaaggtcttttcacctggcccgcatggacacccagaccaggtcccctacatcgtgacctgggaagccttggcttttga
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gagatcttatatggggcacccccgccccttgtaaacttccctgaccctgacatgacaagagttactaacagcccctctct
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accgaccggtggtacctcacccttaccgagtcggcgacacagtgtgggtccgccgacaccagactaagaacctagaacct
cgctggaaaggaccttacacagtcctgctgaccacccccaccgccctcaaagtagacggcatcgcagcttggatacacgc
cgcccacgtgaaggctgccgaccccgggggtggaccatcctctagactgccGGATCTCGAGGGATCCTCCCCAGCATGCC

TGCTATTGTCTTCCCAATCCTCCCCCTTGCTGTCCTGCCCCACCCCACCCCCCAGAATAGAATGACACCTACTCAGACAA

TGCGATGCAATTTCCTCATTTTATTAGGAAAGGACAGTGGGAGTGGCACCTTCCAGGGTCAAGGAAGGCACGGGGGAGGG

GCAAACAACAGATGGCTGGCAACTAGAAGGCACAGTCGAGGtCTAGCTTGCCAAACCTACAGGTGGGGTCTTTCATTCCC

FIG._12A

CCCTTTTTCTGGAGACTAAATAAAATCTTTTATTTTatcgatagatcccggtcggcatctactctattcctttgccctcg
gacgagtgctggggcgtcggtttccactatcggcgagtacttctacacagccatcggtccagacggccgcgcttctgcgg
gcgatttgtgtacgcccgacagtcccggctccggatcggacgattgcgtcgcatcgaccctgcgcccaagctgcatcatc
gaaattgccgtcaaccaagctctgatagagttggtcaagaccaatgcggagcatatacgcccggagccgcggcgatcctg
caagctccggatgcctccgctcgaagtagcgcgtctgctgctccatacaagccaaccacggcctccagaagaagatgttg
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cctgtgcacggcgggagatgcaataggtcaggctctcgctaaattccccaatgtcaagcacttccggaatcgggagcgcg
gccgatgcaaagtgccgataaacataacgatctttgtagaaaccatcggcgcagctatttacccgcaggacatatccacg
ccctcctacatcgaagctgaaagcacgagattcttcgccctccgagagctgcatcaggtcggagacgctgtcgaactttt
cgatcagaaacttctcgacagacgtcgcggtgagttcaggcttttttcatggtattatcatcgtgtttttcaaaggaaaac
cacgtccccgtggttcgggggggcctagacgtttttttaacctcgactaaacacatgtaaagcatgtgcaccgaggccccag
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ccgcagaggcacctgtcgccaggtgggggttccgctgcctgcaaagggtcgctacagacgttgtttgtcttcaagaagc
ttCCAGAGGAACTGCTTCCTTCACGACATTCAACAGACCTTGCATTCCTTTGGCGAGAGGGGAAAGACCCctagactaga

ccaagctttggatttcatttctgaagtttgaattttctgagtcactagtaatgtccttgaggatgatagtctgaattttc
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tcaacatcagataaatttattgccactgtttcaggatttaaggttggagattcatgagaaccttggttttcctttctgtg
ctttctgcatgttttctgtacttcctttctcttcacccaaacaattagtggaattggcaaaagaagaagacaaagccacc
ccaaccggTTTCTGGGACTTTGTTTCCTGCAGTTTGTATTGCTGGTTGCTGTGCATGGCTCAAGGGTTCCATGTTCACAC

GAGGCGCAGCGAACACAGTGTTCACAGCCAGGAGAATCGCAGTAGAAGTCTGGTTTGCACTTGCACTTGGTATTCTGGGT

CAGGGTGCAGTTTGTTTCCACTTCTAAACCATGCTCTTCATCGCAGAGTGTGCATCTTCTGCATTTATCAGCATAATGGT

TCTTGTCCATGTACTCCTTCCCTTCTGTGCATGGGGCACAGGTTGGTGTACCCCCATTCATTTTGCAGTCCTCAACTTTT

TTTTTACCAGGTTGGCATGGTTGACAGCAAAATGGGCCTCCTTGATATAATCCTTCTGAGCAGTTTTTATCAGTTTCATG

AACCCGCCTCCTCAGCTTTAAACTCTCGGAGATGCTATTAGTACCTTGAGTATGAACTCTTAACTGTGAGCCAGCAAGCA

FIG._12B

CCAGAGGCAGGACAGCCCAGATCCACACCATgGTGGCTTTACCAACAGTACCGGAATGCCAAGCTTGCGGCCGCTTAAGA

GCTGTAATTGAACCTGGGAGTGGACACCTGTGGAGAGAAAGGCAAAGTGGATGTCAGTAAGACCAATAGGTGCCTATCAG

AAACGCAAGAGTCTTCTCTGTCTCGACAAGCCCAGTTTCTATTGGTCTCCTTAAACCTGTCTTGTAACCTTGATACTTAC

CTGCCCAGTGCCTCACGACCAACTTctgcaggaattcctggacagctcccagatgatcagtaaccgtggttgttatttct
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cgcactgaggtgaactggccctcggggGcgcgtgtcccagatgtgtgtgcagggcctcctgatggccgcagccctcgtcc
ctgtgacccgcttggagctggcaccctgagtggtggcctcacCTTGTACTCACTCCCAGGTCACTGTCCtcgacGCGGCC

GCTCGAcgatAAAATAAAAGATTTTATTTAGTCTCCAGAAAAAGGGGGGAATGAAAGACCCCACCTGTAGGTTTGGCAAg

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TGTATCCAATAAACCCTCTTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGA

CTACCCGTCAGCGGGGGTCTTTCAcatgcaGCATGTATCAAAATTAATTTGGTTTTTTTTCTTAAGTATTTACATTAAAT

GGCCATagtttcGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAG

CCGGAAGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCT

TTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCG

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AAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAG

GTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCC

FIG._12C

TGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTC

AGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGG

TAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAG

CGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATC

TGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGG

TGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGT

CTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTT

TTAAATTAAAAATGAAGTTTGCGCAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAAT

CAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGA

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CCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCAC

GCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAA

AAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGC

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aatagtgtatgcggcgaccgagttgctcttgcccggcgtcaacacgggataataccgcgccacatagcagaactttaaaa
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cactcgtgcacccaactgatcttcagcatcttttactttcaccagcgtttctgggtgagcaaaaacaggaaggcaaaatg
ccgcaaaaaagggaataagggcgacacggaaatgttgaatactcatactcttcctttttcaatattattgaagcatttat
cagggttattgtctcatgacattaacctataaaaataggcgt

FIG._12D

atcacgaggccctttcgtcttcaagaacagctttgctcttaggagtttcctaatacatcccaaactcaaatatataaagc
atttgacttgttctatgccctagttattaatagtaatcaattacggggtcattagttcatagcccatatatggagttccg
cgttacataacttacggtaaatggcccgcctggctgaccgcccaacgacccccgcccattgacgtcaataatgacgtatg
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TGCGATGCAATTTCCTCATTTTATTAGGAAAGGACAGTGGGAGTGGCACCTTCCAGGGTCAAGGAAGGCACGGGGGAGGG

GCAAACAACAGATGGCTGGCAACTAGAAGGCACAGTCGAGGtCTAGCTTGCCAAACCTACAGGTGGGGTCTTTCATTCCC

FIG._13A

CCCTTTTTCTGGAGACTAAATAAAATCTTTTATTTTatcgatagatcccggtcggcatctactctattcctttgccctcg
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CTGTCTCGACAAGCCCAGTTTCTATTGGTCTCCTTAAACCTGTCTTGTAACCTTGATACTTACCTGCCCAGTGCCTCACG

FIG._13B

ACCAACTTctgcaggaattcctggacagctcccagatgatcagtaaccgtggttgttatttctgtgccgggcagtggagc
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CCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGT

FIG._13C

GCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCC

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GAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAG

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FIG._13D

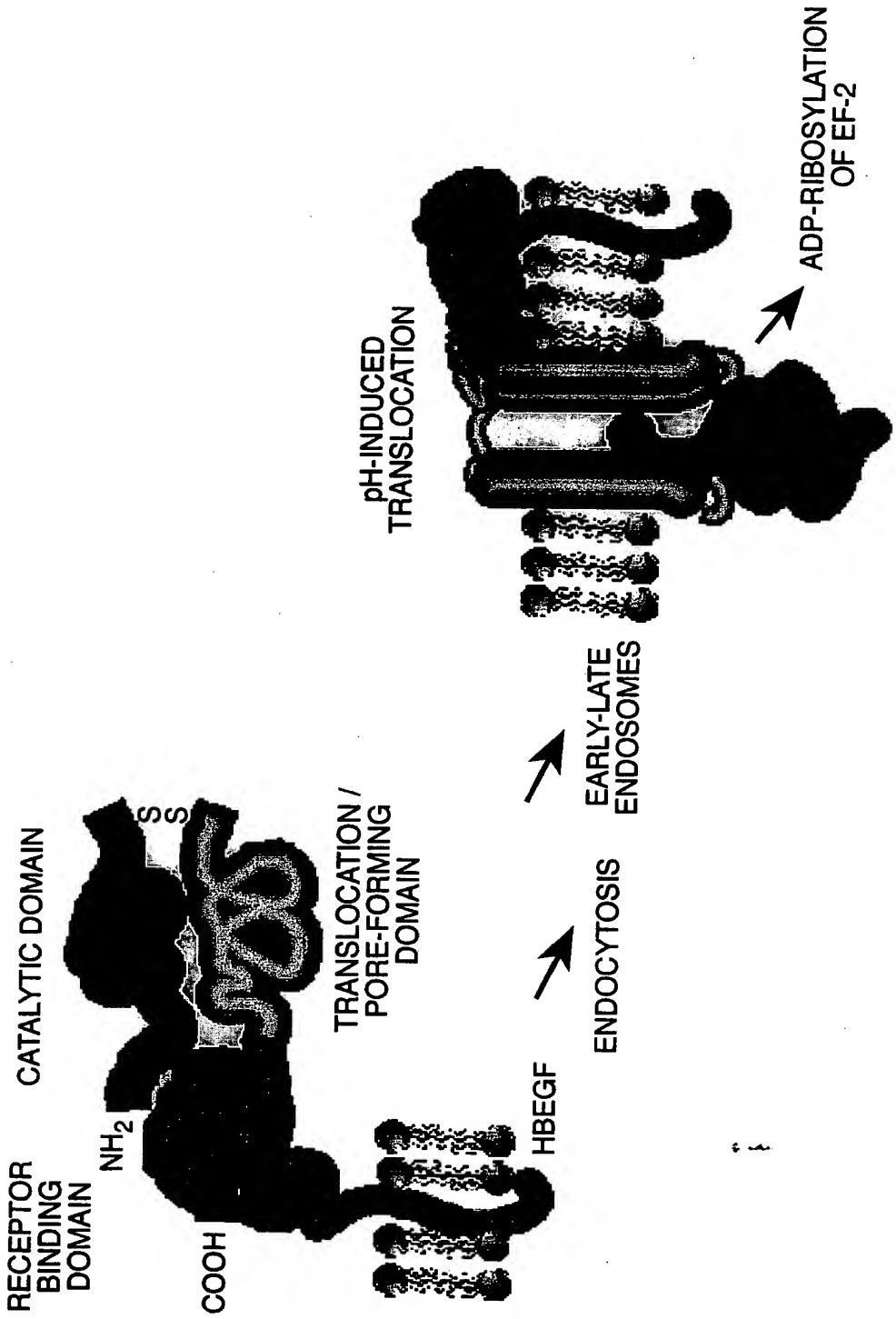
RECEPTOR BINDING DOMAIN
CATALYTIC DOMAIN
NH_2
COOH
S
S
TRANSLOCATION / PORE-FORMING DOMAIN
HBEGF
ENDOCYTOSIS
EARLY-LATE ENDOSOMES
pH-INDUCED TRANSLOCATION
ADP-RIBOSYLATION OF EF-2

FIG._14

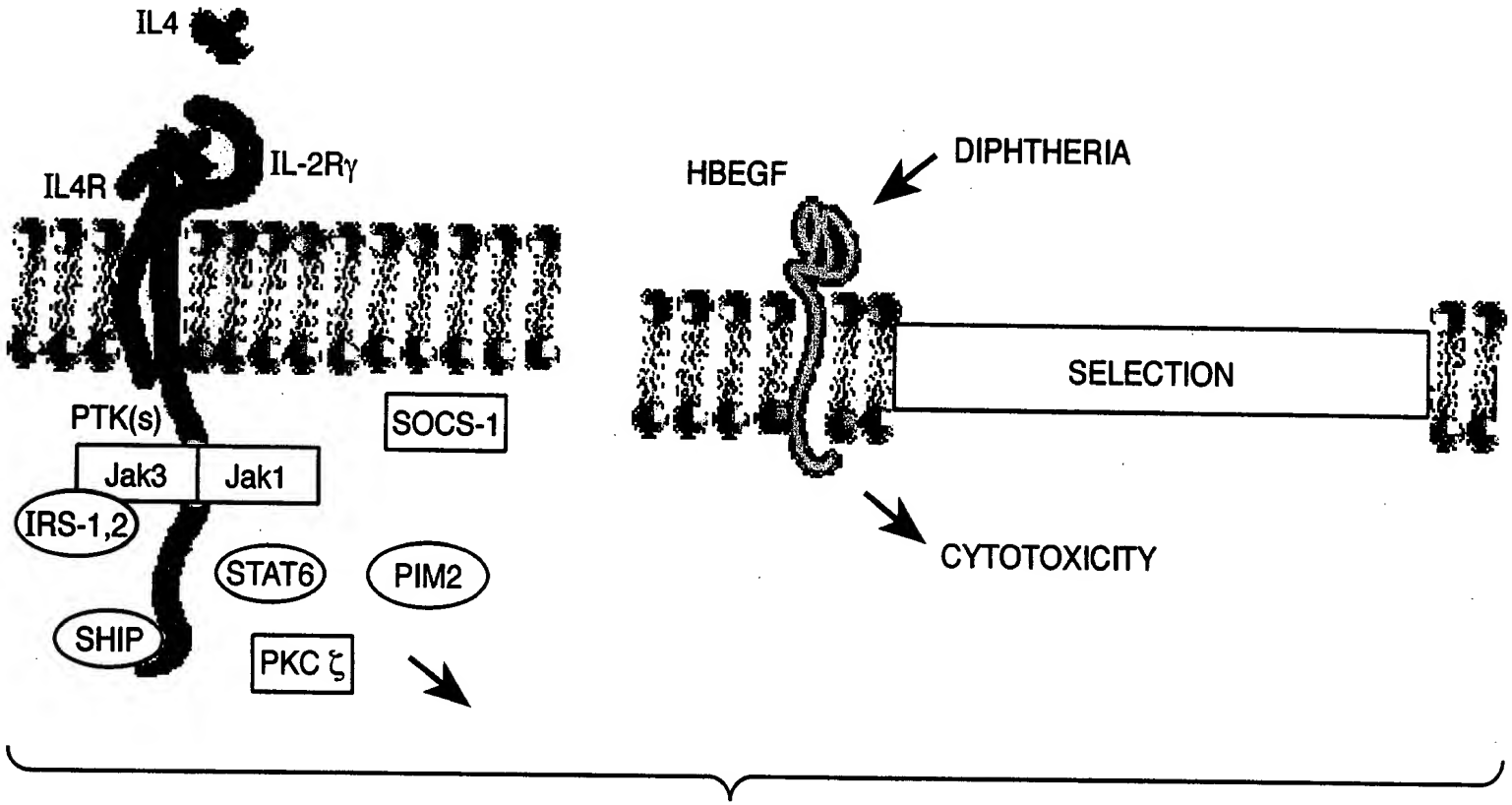

FIG._15A

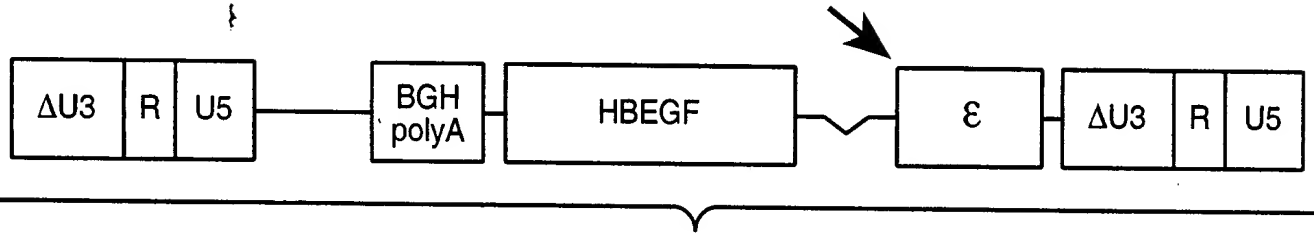

FIG._15B

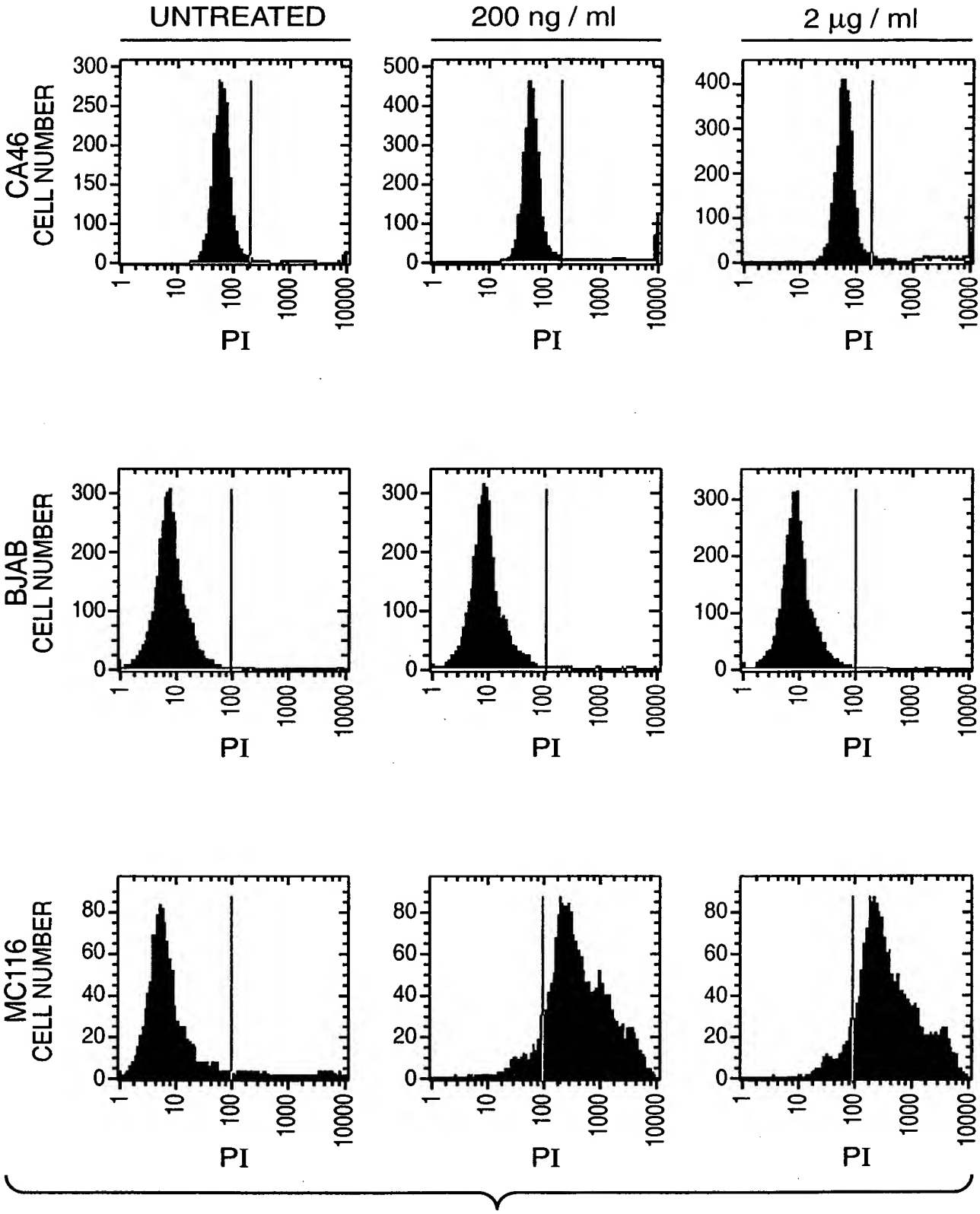
UNTREATED
200 ng / ml
2 µg / ml
CA46
CELL NUMBER
BJAB
CELL NUMBER
MC116
CELL NUMBER
PI
PI
PI
PI
PI
PI
PI
PI
PI

FIG._16

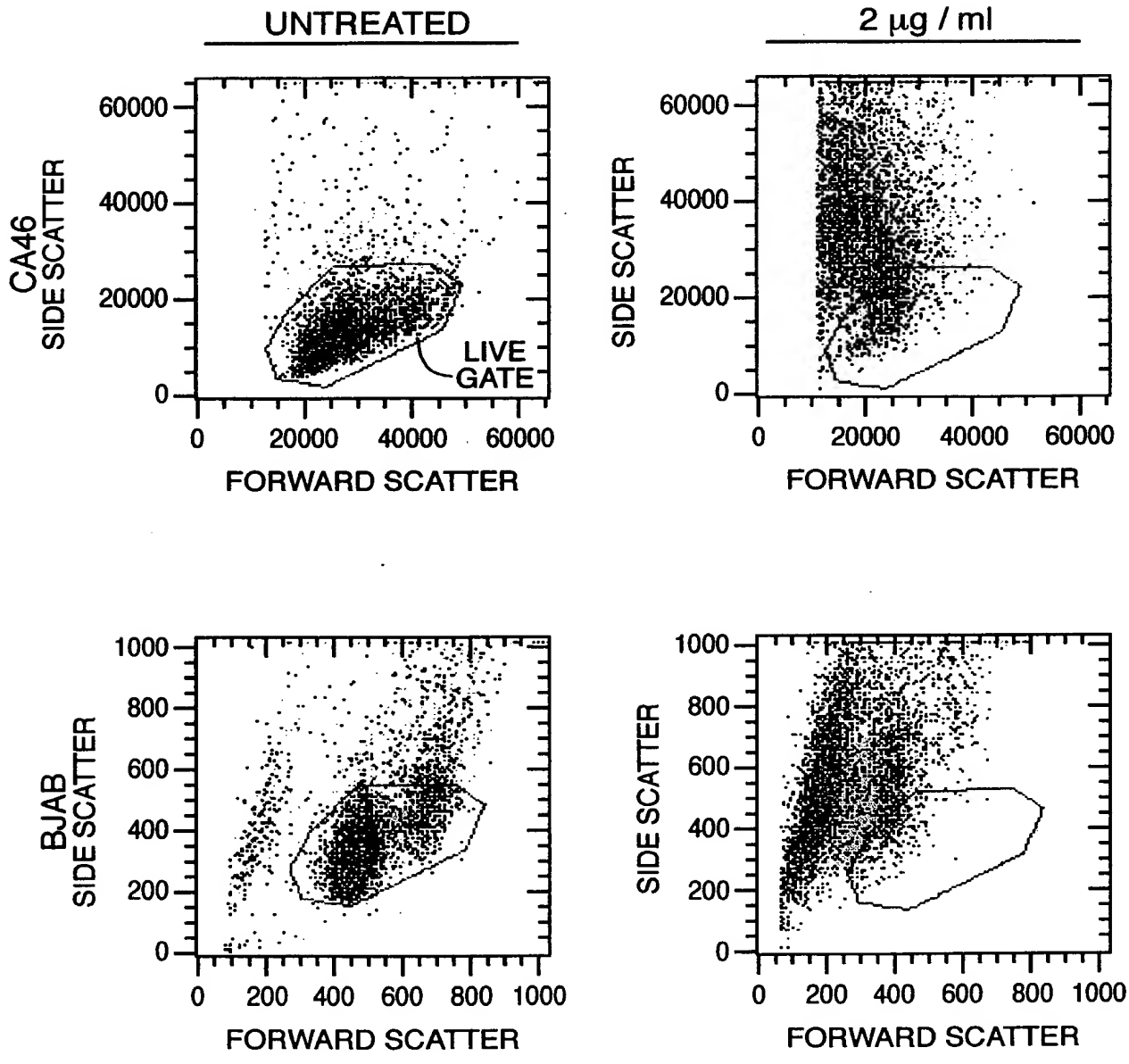
UNTREATED
2 µg / ml
CA46
SIDE SCATTER
BJAB
SIDE SCATTER
SIDE SCATTER
FORWARD SCATTER
LIVE
GATE
0
20000
40000
60000
200
400
600
800
1000

FIG._17

FIG._18A

FIG._18B

FIG._18C

FIG._18D

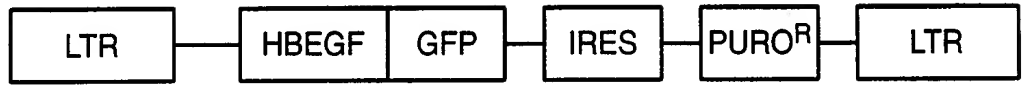

FIG._18E

FIG._18F

FIG._18G

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